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Total Number of Pages in This Submission

22

Application Number	10/636,148
Filing Date	August 7, 2003
First Named Inventor	Bohling et al.
Art Unit	1711
Examiner Name	Irina S. Zemel
Attorney Docket Number	A01406

ENCLOSURES (Check all that apply)

- ☐ Fee Transmittal Form
- ☐ Fee Attached
- ☐ Amendment/Reply
 - ☐ After Final
 - ☐ Affidavits/declaration(s)
- ☐ Extension of Time Request
- ☐ Express Abandonment Request
- ☐ Information Disclosure Statement
- ☐ Certified Copy of Priority Document(s)
- ☐ Reply to Missing Parts/Incomplete Application
 - ☐ Reply to Missing Parts under 37 CFR 1.52 or 1.53

- ☒ Drawing(s)
- ☐ Licensing-related Papers
- ☐ Petition
- ☐ Petition to Convert to a Provisional Application
- ☐ Power of Attorney, Revocation
- ☐ Change of Correspondence Address
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- ☐ Request for Refund
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- ☐ After Allowance Communication to TC
- ☐ Appeal Communication to Board of Appeals and Interferences
- ☒ Appeal Communication to TC (Appeal Notice, Brief, Reply Brief)
- ☐ Proprietary Information
- ☐ Status Letter
- ☒ Other Enclosure(s) (please identify below):

Declaration Under 37 C.F.R.
§1.132 - James C. Bohling

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name Rohm and Haas Company

Signature *Kenneth Crimaldi*

Printed name Kenneth Crimaldi

Date August 17, 2005

Reg. No. 40,968

CERTIFICATE OF TRANSMISSION/MAILING

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Typed or printed name Janice Soulas

Date 8-22-05

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GROUP ART UNIT: 1711

APPEAL NO. _____

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF APPEALS AND INTERFERENCES**

APPEAL BRIEF

In re the Application of BOHLING et al.

Filed: August 7, 2003

Serial No. 10/636,148

For: RESIN FOR SOLID PHASE SYNTHESIS

Kenneth Crimaldi
Attorney for Appellants

Irina S. Zemel
Examiner

Enclosed:
Transmittal Form
Declaration Under 37 C.F.R. §1.132
Drawings (Figs. 1 – 5)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: BOHLING et al. :
:
Application No.: 10/636,148 : Group No.: 1711
:
Filed: August 7, 2003 : Examiner: Irina S. Zemel
:
For: RESIN FOR SOLID PHASE SYNTHESIS :

MAIL STOP APPEAL BRIEF - PATENTS
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Alexandria, VA 22313-1450

APPEAL BRIEF

This is an appeal from the rejection dated February 23, 2005 finally rejecting claims 1-6 and 8-10. The rejected claims are set out in the Appendix. Appellants filed a Notice of Appeal pursuant to 37 C.F.R. § 1.191 on May 10, 2005.

(1) Real Party In Interest

The owner of the present application and the invention contained therein is ROHM AND HAAS COMPANY.

(2) Related Appeals, Interferences or Judicial Proceedings

No appeals, interferences or judicial proceedings are known to appellants, the appellants' legal representative, or the assignee which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status Of Claims

The status of the claims is as follows:

Claims pending: 1-6 and 8-10

Allowed claims: none

Claims objected to: none

Claims canceled: 7

Claims rejected: 1-6 and 8-10

Claims on appeal: 1-6 and 8-10

Claims withdrawn from consideration by the Examiner: none.

(4) Status Of Amendments after Final Rejection

Appellants have not filed an amendment after final rejection in the present application.

(5) Concise Explanation of Invention for each Independent Claim

Claim 1: The present invention provides a crosslinked polymeric bead comprising a polymer having from 0.5 mole percent to 2 mole percent crosslinker; wherein said bead has a diameter no greater than 200 μm , no void spaces having a diameter greater than 5 μm , and less than 5 weight percent of organic extractables. [page 1, lines 22-25]

Claim 6: The present invention is further directed to a method for producing a lightly crosslinked polymeric bead having no void spaces having a diameter greater than 5 μm [page 1, lines 26-27]; said method comprising steps of:

(a) preparing a suspension polymerization mixture in a vessel; said mixture comprising: (i) a monomer mixture comprising at least one vinyl monomer and 0.5 mole percent to 2 mole percent of at least one crosslinker [page 1, lines 28-30 & 22-23]; and (ii) from 0.25 mole percent to 1.5 mole percent of at least one free radical initiator; [page 1, lines 30-31]

(b) removing oxygen from the suspension polymerization mixture and the vessel by introducing an inert gas for a time sufficient to produce an atmosphere in the vessel containing no more than 5 percent oxygen; [page 1, lines 31-32]

(c) allowing the monomer mixture to polymerize; [page 1, line 33] and

(d) washing the bead with an aprotic organic solvent. [page 1, lines 33-34]

Claim 10: The present invention is further directed to a lightly crosslinked polymeric bead having no void spaces having a diameter greater than 5 μm [page 1, lines 26-27]; said bead produced by a method comprising steps of:

(a) preparing a suspension polymerization mixture in a vessel; said mixture comprising: (i) a monomer mixture comprising at least one vinyl monomer and 0.5 mole percent to 2 mole percent of at least one crosslinker [page 1, lines 28-30 & 22-23]; and (ii) from 0.25 mole percent to 1.5 mole percent of at least one free radical initiator; [page 1, lines 30-31]

(b) removing oxygen from the suspension polymerization mixture and the vessel by introducing an inert gas for a time sufficient to produce an atmosphere in the vessel containing no more than 5 percent oxygen; [page 1, lines 31-32]

(c) allowing the monomer mixture to polymerize; [page 1, line 33] and

(d) washing the bead with an aprotic organic solvent. [page 1, lines 33-34]

(6) Grounds of Rejection to be Reviewed on Appeal

Claims 1-6 and 8-10 stand rejected under 35 USC § 103(a) as being obvious over Meitzner et al. (U.S. Pat. No. 4,486,313).

(7) Argument

Regarding whether or not claims 1-6 and 8-10 are unpatentable under 35 USC § 103(a) over Meitzner et al. (U.S. Pat. No. 4,486,313; "Meitzner"):

A. Meitzner Fails to Suggest Several Limitations of the Present Claims

All claim limitations must be taught or suggested in the prior art. *In re Royka*, 490 F.2d 981 (C.C.P.A. 1974). Limitations of independent claims 1, 6 and 10 are not taught or suggested in Meitzner, namely that the polymeric bead has: (i) from 0.5 mole percent to 2 mole percent crosslinker (all claims); (ii) no void spaces having a diameter greater than 5 μm (all claims); (iii) a diameter no greater than 200 μm (claim 1); and (iv) less than 5 weight percent of organic extractables (claim 1).

1. Regarding limitation (i): Meitzner is directed to preparation of highly crosslinked beads, and teaches use of a minimum crosslinker level of 4 to 6%, with a maximum of 25% (Col. 5, lines 20-30). Meitzner fails to suggest, or even to mention any crosslinker level below 4%. A finding of obviousness under 35 U.S.C. § 103(a) requires that the reference must suggest the desirability of the particular modifications needed to arrive at the claimed invention. *In re Gordon*, 733 F.2d 900 (Fed. Cir. 1984). The final rejection states only that it “would have been clearly obvious for an ordinary artisan to achieve desired physical properties of a polymer depending of its end use since it is well known on the art that varying the amount of crosslinker ‘has a profound effect on the physical properties of the product’” (page 3). Meitzner’s general disclosure that varying crosslinking will result in a change in properties hardly amounts to a suggestion of the specific range “from 0.5 mole percent to 2 mole percent crosslinker,” much less a suggestion even to vary properties in a direction that could result in Applicants’ invention. Meitzner contains no guidance as to the optimum ranges of crosslinker that would achieve the beads claimed by Applicants; rather, the disclosure is, at most, an invitation to experiment with crosslinker level. The notion that obviousness can result from leaving those skilled in the art to find the claimed invention via undirected experimentation, i.e., that it would be “obvious to try” the claimed parameters, has been rejected repeatedly by the Federal Circuit. *See, e.g., In re Fine*, 837 F.2d 1071 (Fed. Cir. 1988).

2. Regarding limitation (ii): Meitzner contains no disclosure at all related to beads with “no void spaces having a diameter greater than 5 μm .” The final rejection first attempts to find a suggestion in Meitzner to omit the “precipitant” used to produce macroporous beads, and then the rejection asserts that this would result in a polymer “with no microchannels.” First, Meitzner distinguishes a microchannel produced by precipitant from the micropores that Meitzner states are “present in all crosslinked polymers” (Col. 5, lines 6-9). Thus, Meitzner does not even recognize the possibility of making polymer beads substantially free of micropores (void spaces). Second the alleged suggestion to omit precipitant in Meitzner is cited as occurring at Col. 4, line 61 to Col. 5, line 23. This passage is merely a discussion of the mechanism by which the precipitant produces microchannels, and in no way suggests that it be omitted.

3. Regarding limitations (iii) and (iv): These limitations of claim 1 are not suggested by Meitzner, and since they are not even mentioned in the final rejection, or the first rejection, the Office has not met its burden of demonstrating that the prior art teaches or suggests all the limitations of claim 1. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).

B. Meitzner Teaches Away from the Present Claims

Meitzner is directed to preparation of beads having large pore spaces (macroreticular structure) by incorporating large amounts of “precipitant” (solvent) and a high level of crosslinker, as cited in A.1. above. The first rejection cites Col. 7, line 56 et seq. as suggesting a modification of the cited crosslinker level. However, at Col. 7, lines 57-58, Meitzner says that the amount of crosslinker “may be varied widely within the scope of the present invention.” (emphasis added) This qualification strictly limits the teaching of Meitzner to crosslinker amounts of no less than 4%, the lowest level within the scope of Meitzner. The other alleged suggestions to modify crosslinker level, as described in A.1. above, do not negate this specific direction not to use crosslinker levels below 4%. Thus, Meitzner not only does not suggest using smaller amounts of crosslinker, it actually teaches away from doing so.

C. One Skilled in the Art Would Have Had No Reasonable Expectation of Success

A prima facie case of obviousness requires that one skilled in the art would have had a reasonable expectation of success in light of the prior art. *In re Dow Chemical*, 837 F.2d 469 (Fed. Cir. 1988). Since, as discussed above, Meitzner contains no guidance as to how to vary the relevant parameters to arrive at the individual claimed limitations, it cannot possibly provide any reasonable expectation of success for the combination. For example, there is no suggestion in Meitzner to lower crosslinker level while also removing the large amounts of precipitant employed by Meitzner. The final rejection cites an experiment in Meitzner in which porogen was omitted (Table II, first entry). However, this experiment was carried out with 20% crosslinker. There is no suggestion anywhere in Meitzner to vary both crosslinker and precipitant levels in combination to prepare a bead having low levels of both. Moreover, Applicants claim beads with no void spaces having a diameter greater than 5 μm . As described above in A.2., Meitzner teaches control of microchannels, but does not even recognize the possibility of reducing micropores in polymers. One skilled in the art certainly could not acquire a reasonable expectation of eliminating micropores larger than 5 μm from this teaching, but would learn only that the occurrence of microchannels could be controlled, but that micropores are not affected by altering any of the relevant parameters. Moreover, there is no indication that this could be achieved at lower crosslinker levels. In short, there is no guidance in Meitzner that reasonably could lead one skilled in the art to make the presently claimed combination of parameters, or to expect it to work. "It is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art." *In re Wesslau*, 353 F.2d 238, 241 (C.C.P.A. 1965). What Meitzner "fairly suggests to one of ordinary skill in the art" is that, in the presence of high levels of crosslinker, precipitant can be added to create microchannels and lower density.

Even, assuming *arguendo*, that Meitzner would teach one skilled in the art the individual limitations of the present claims, there is nothing in Meitzner that would provide a reasonable expectation of success in using the particular claimed combination.

D. Applicants Have Obtained Unexpected Results

The Declaration of Dr. James C. Bohling, submitted with Applicants' response filed November 15, 2004, demonstrates that beads having 2% crosslinker and a precipitant, according to Meitzner's procedure, do not meet the void space limitation of the present claims. Paragraph 7 of the Declaration summarizes the key points of the Figures therein. Figure 1 shows that beads made according to the present invention are completely free of visible void spaces. In contrast, Figures 2-5 show that beads prepared by the Meitzner method, but at low crosslinker levels, have numerous void spaces larger than 5 μm . The central teaching of Meitzner is the use of precipitants, and there is no suggestion to use lower crosslinker levels or to omit the precipitant. Moreover, Meitzner does not recognize that it would be possible to prepare polymeric beads without micropores larger than 5 μm . Therefore, the improved properties of beads made according to the present invention could not have been predicted from Meitzner.

CONCLUSION

Based on the foregoing, Appellants respectfully submit that the pending claims are currently in condition for allowance. Appellants respectfully request the Board to pass the pending claims to allowance.

Enclosed herewith, Appellants have filed a Certificate of Mailing to establish the timely filing of this Appeal Brief.

The Commissioner is hereby authorized to charge any additional fee which may

10/636,148
August 15, 2005

A01406

be required, or to credit any overpayments to Deposit Account 18-1850.

Respectfully submitted,

A handwritten signature in cursive script, appearing to read "Kenneth Crimaldi".

Kenneth Crimaldi
Attorney for Appellants
Registration No. 40,968

ROHM AND HAAS COMPANY
100 Independence Mall West
Philadelphia, PA 19106-2399
August 15, 2005

APPENDIX A: Copy of the Appealed Claims

1. A crosslinked polymeric bead comprising a polymer having from 0.5 mole percent to 2 mole percent crosslinker; wherein said bead has a diameter no greater than 200 μm , no void spaces having a diameter greater than 5 μm , and less than 5 weight percent of organic extractables.
2. The crosslinked polymeric bead of claim 1 in which the polymer has from 0.5% to 1.6% crosslinker and the bead has a diameter no greater than 170 μm .
3. The crosslinked polymeric bead of claim 2 in which the polymer is a styrene polymer with a divinylbenzene crosslinker.
4. The crosslinked polymeric bead of claim 3 in which the polymer has from 0.7 mole percent to 1.2 mole percent crosslinker and the bead has no void spaces having a diameter greater than 3 μm , and less than 3 weight percent of organic extractables.
5. The crosslinked polymeric bead of claim 4 in which the bead has a diameter no greater than 150 μm .
6. A method for producing a lightly crosslinked polymeric bead having no void spaces having a diameter greater than 5 μm ; said method comprising steps of:
 - (a) preparing a suspension polymerization mixture in a vessel; said mixture comprising: (i) a monomer mixture comprising at least one vinyl monomer and 0.5 mole percent to 2 mole percent of at least one crosslinker; and (ii) from 0.25 mole percent to 1.5 mole percent of at least one free radical initiator;
 - (b) removing oxygen from the suspension polymerization mixture and the vessel by introducing an inert gas for a time sufficient to produce an atmosphere in the vessel containing no more than 5 percent oxygen;

- (c) allowing the monomer mixture to polymerize; and
- (d) washing the bead with an aprotic organic solvent.

8. The method of claim 6 in which the atmosphere in the vessel contains no more than 2 percent oxygen.

9. The method of claim 8 in which said at least one vinyl monomer comprises at least 90 mole percent styrene, said at least one crosslinker comprises divinylbenzene, and the bead has a diameter no greater than 200 μm .

10. A lightly crosslinked polymeric bead having no void spaces having a diameter greater than 5 μm ; said bead produced by a method comprising steps of:

- (a) preparing a suspension polymerization mixture in a vessel; said mixture comprising: (i) a monomer mixture comprising at least one vinyl monomer and 0.5 mole percent to 2 mole percent of at least one crosslinker; and (ii) from 0.25 mole percent to 1.5 mole percent of at least one free radical initiator;
- (b) removing oxygen from the suspension polymerization mixture and the vessel by introducing an inert gas for a time sufficient to produce an atmosphere in the vessel containing no more than 5 percent oxygen;
- (c) allowing the monomer mixture to polymerize; and
- (d) washing the bead with an aprotic organic solvent.

APPENDIX B: Copy of Declaration under 37 C.F.R. § 1.132

This Declaration was filed on 11/18/04 with an Amendment in response to the first Office Action; it was stamped as received by the USPTO on 11/22/04. A copy of the Declaration is attached.



PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Atty Docket No. A01406

KC

In re application of:
James Charles Bohling et al.

Serial No.: 10/636,148 : Group Art Unit: 1711

Filed: August 7, 2003 : Examiner: Morton Foelak

For: RESIN FOR SOLID PHASE SYNTHESIS

DECLARATION UNDER 37 C.F.R. § 1.132

I, James C. Bohling, of 1904 Stirling Drive, Lansdale, PA, declare and say as follows:

1. I have been employed at the Rohm and Haas Company since 1999. I have a Bachelor of Science degree in Chemistry from Hope College (1992), a Ph.D. in Physical Organic Chemistry from Boston College (1997), and completed Post Doctoral fellowship at the University of Utah (1999). I have been involved with our Ion Exchange Business since 1999 and the Advanced Biosciences business since 2003. My job responsibilities have included research and development in the area of improved resin beads useful in solid-phase organic synthesis. I am currently a Senior Scientist.

2. I have been the coinventor of 19 U.S. patent applications filed during my tenure at Rohm and Haas Company.

3. As a co-inventor of the present invention, I am thoroughly familiar with its subject matter and background. I have read the Official Action dated August 19, 2004 in the above-mentioned US patent application (Serial No. 10/636,148). I have reviewed the cited reference, Meitzner et al.

4. In November, 2004, at the Rohm and Haas Company research laboratories in Spring House, Pennsylvania, I supervised preparation of polymeric beads made by a procedure disclosed in Meitzner, but with an amount of crosslinker within the scope of the present application. Beads were made using 1.5% and 2%

crosslinker, and 35% porogen {4-methyl-2-pentanol (MIBC)); see Meitzner, Col. 8, line 61 to Col. 9, line 2. The details of the procedure are presented below:

Summary of Process Run:

Run process in a 2L round bottom flask with a light nitrogen sweep. Sparge monomer phase with N₂. Stir @ 275 rpm during hold period. Ramp process to 86°C over 60 minutes, hold for 6 hours. Wash with tetrahydrofuran (THF) and methanol.

Preparation of Aqueous Solution:

Weigh 638g of DI water and charge in round bottom flask. Stir @ 150rpm and heat to 80°C under N₂ sweep. Once temperature is reached, charge 3.175g of MHEC- 8000 (hydroxyethyl methyl cellulose) slowly in flask. Hold for 60 minutes @ 80°C. After hold time cool Aqueous solution to 25°C - 30°C. Weigh out and charge the following to the flask: 0.036g WA-100 (sodium lauryl sulfate). Stir for 30 minutes. Sweep with N₂.

Preparation of Monomer Solution:

Prepare monomer in a beaker, charge the following:

For 2% DVB: 10.6g DVB-55% (divinylbenzene), 279.6g styrene, 3.87g of 75% benzoyl peroxide (2.90g active) and 156g of 4-methyl-2-pentanol (MIBC);
For 1.5% DVB: 7.9g DVB-55% (divinylbenzene), 282.3g styrene, 3.87g of 75% benzoyl peroxide (2.90g active) and 156g of 4-methyl-2-pentanol (MIBC).

Adjust agitator speed to 275rpm before charging monomer mix to flask. Stop agitator and charge monomer to Aqueous solution. After charging monomer mix resume agitation and stir for 30 minutes @ 25°C. Ramp temperature to 86°C over 1 hour. Hold @ 86°C for 6 hours.

Washing:

After cooling place resin into Buchner funnel and wash with 8 bed volumes of THF followed by 4 bed volumes of methanol with stirring while draining. Dry the resin in vacuum oven and screen to 150-90 micron.

5. In August, 2002, I obtained beads made on a commercial scale in Soma, Japan by scaling up the procedure of the present invention, as shown below:

Summary of Process Run:

Run process in a 2L round bottom flask with a light nitrogen sweep. Sparge monomer phase with N₂. Stir @ 275 rpm during hold period. Ramp process to 84°C over 60 minutes, hold for 12 hours. Treat with Cellulase for 4 hours.

Preparation of Aqueous Solution:

Weigh 638g of DI water and charge in round bottom flask. Stir @ 150rpm and heat to 80°C under N₂ sweep. Once temperature is reached, charge 3.175g of MHEC- 8000 slowly in flask. Hold for 60 minutes @ 80°C. After hold time cool Aqueous solution to 25°C - 30°C. Weigh out and charge the following to the

flask: 2.4 g 50% NaOH, 2.5g Boric Acid, 0.036g WA-100(SLS), and 0.1g Sodium Nitrite. Stir for 30 minutes.

Preparation of Monomer Solution:

Prepare monomer in a beaker, charge the following: 6.55g DVB (Divinylbenzene), 440.0g Styrene, 5.8g Trigonox (Trig 21). Transfer mix to an Addition Funnel and sparge for 40 minutes.

Adjust agitator speed to 275rpm before charging monomer mix to flask. Stop agitator and charge monomer to Aqueous solution. Position Addition Funnel over flask so as not to introduce air to monomer solution. After charging monomer mix resume agitation and stir for 30 minutes @ 25° C. Ramp temperature to 84° C over 1 hour. Hold @ 84° C for 12 hours.

Cellulase Treatment:

After 12 hour hold cool batch to 45° C, adjust pH to 5.0 with HCL. (37%) Charge 19.05g of Cellulase 4000 to batch, stir for 2 hours @ 45° C. After the 2 hour hold add a second charge of Cellulase 4000 and hold for 2 hours @ 45° C. At the end of hold period cool down to room temperature, remove from flask and wash with DI water.

6. Beads produced by the foregoing procedures were compared, using light microscopy. Beads were prepared for microscopy by placing them, dry, onto a microscope slide and analyzing on a Standard Zeiss Stemi 2000C microscope, with the images captured with a Media Cybernetics Cool Snap Digital camera and Image Pro 4 software. Photos were obtained at 10x, (both 5x and 2x lenses in place). Light was transmitted indirectly from below.

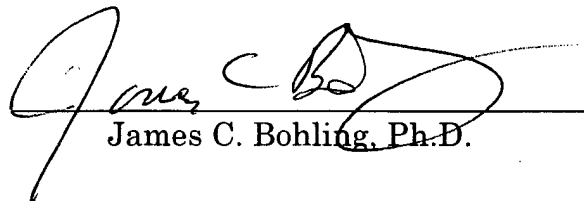
7. Photomicrographs are attached as Figures 1 to 5. Identification of the figures is as follows:

	Crosslinker (DVB)	Porogen (MIBC)	Comments
Figure 1	1%	0%	method of present application
Figure 2	1.5%	35%	Meitzner process, 1.5% DVB
Figure 3	1.5%	35%	enlargement of Fig. 2
Figure 4	2%	35%	Meitzner process, 2% DVB
Figure 5	2%	35%	Meitzner process, 2% DVB

Each Figure bears a calibration line to indicate the scale of objects in the photograph.

8. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful

false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United State Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

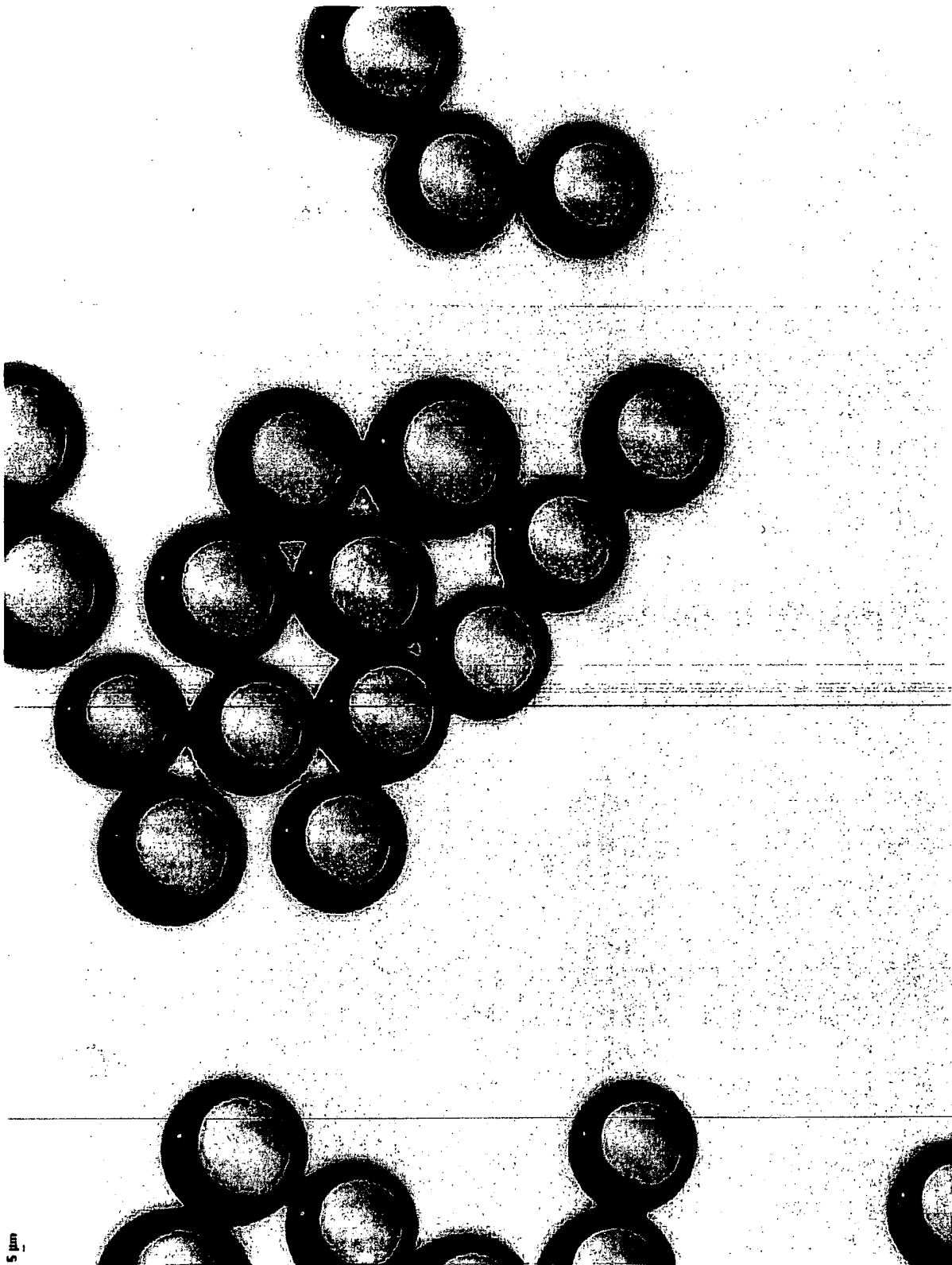


James C. Bohling, Ph.D.

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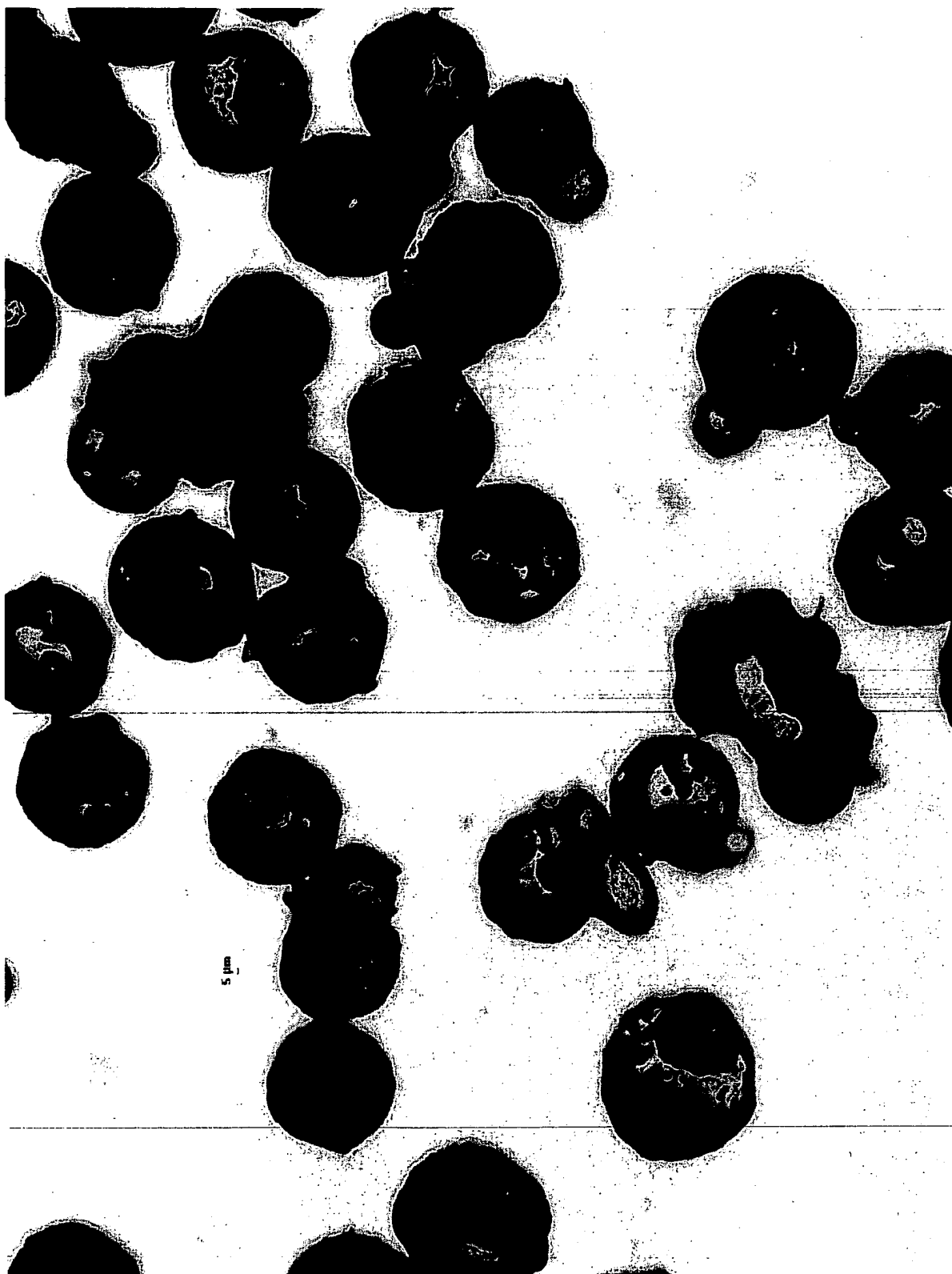
Date: November 15 , 2004

Figure 1



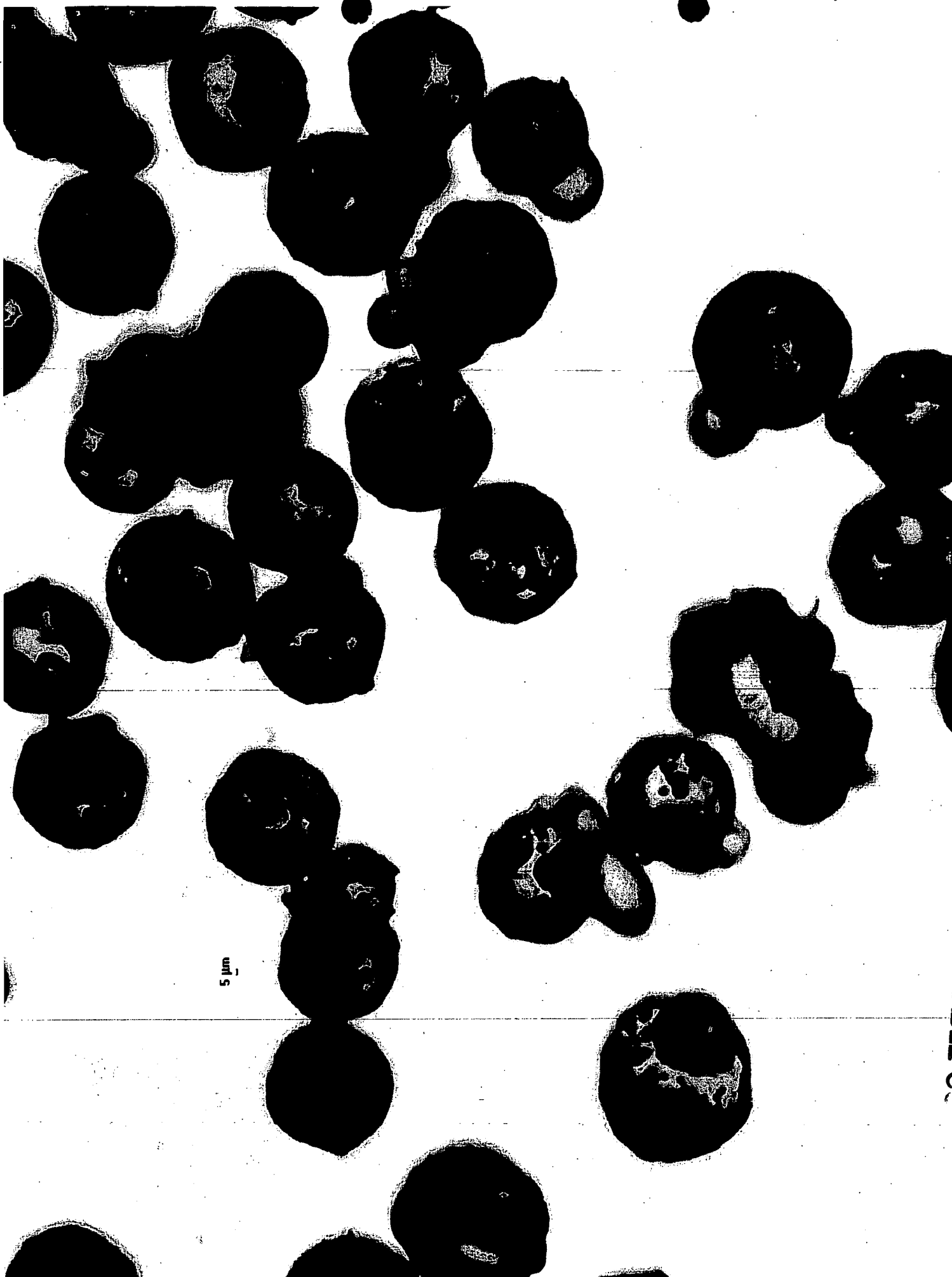
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Figure 2



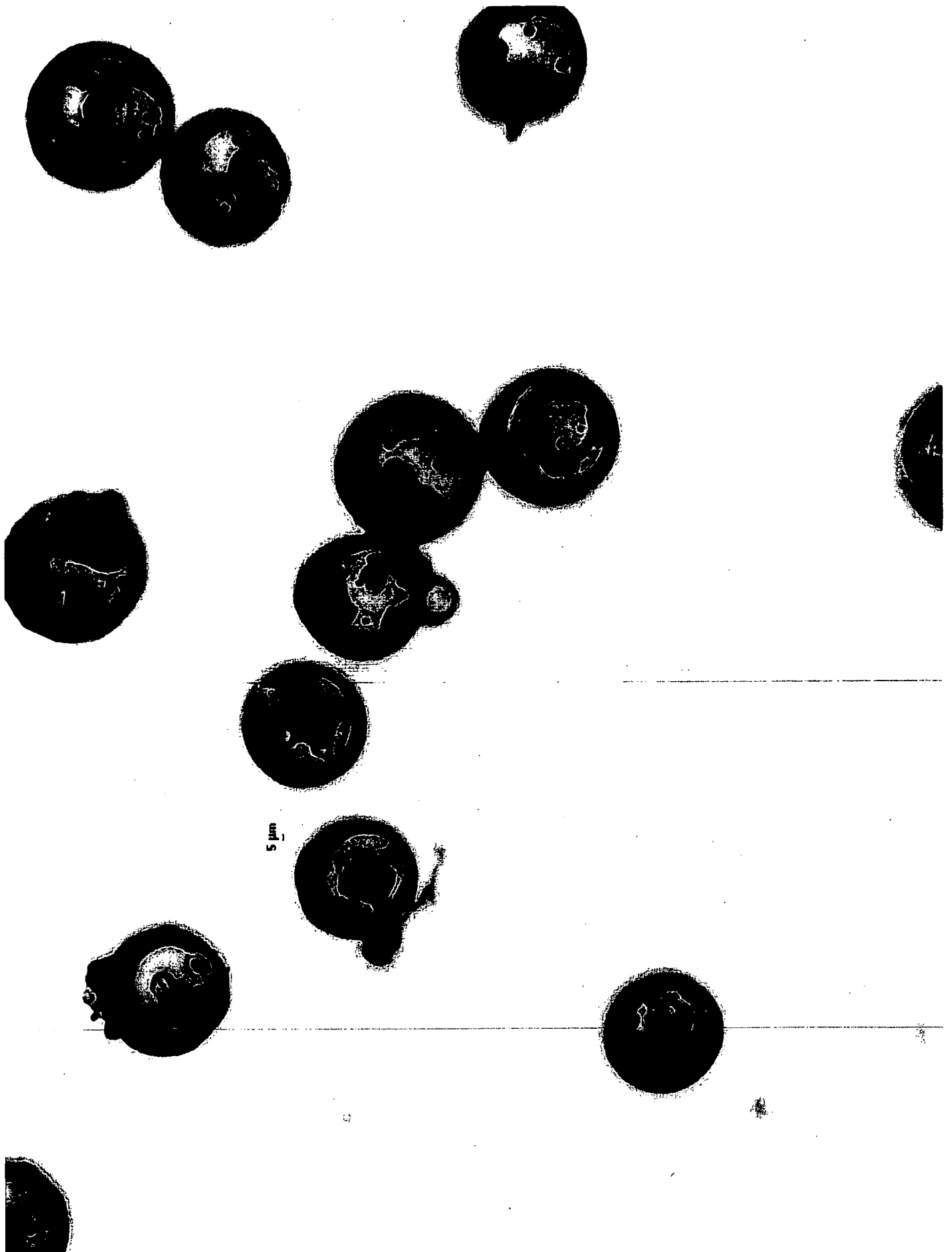
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Figure 3



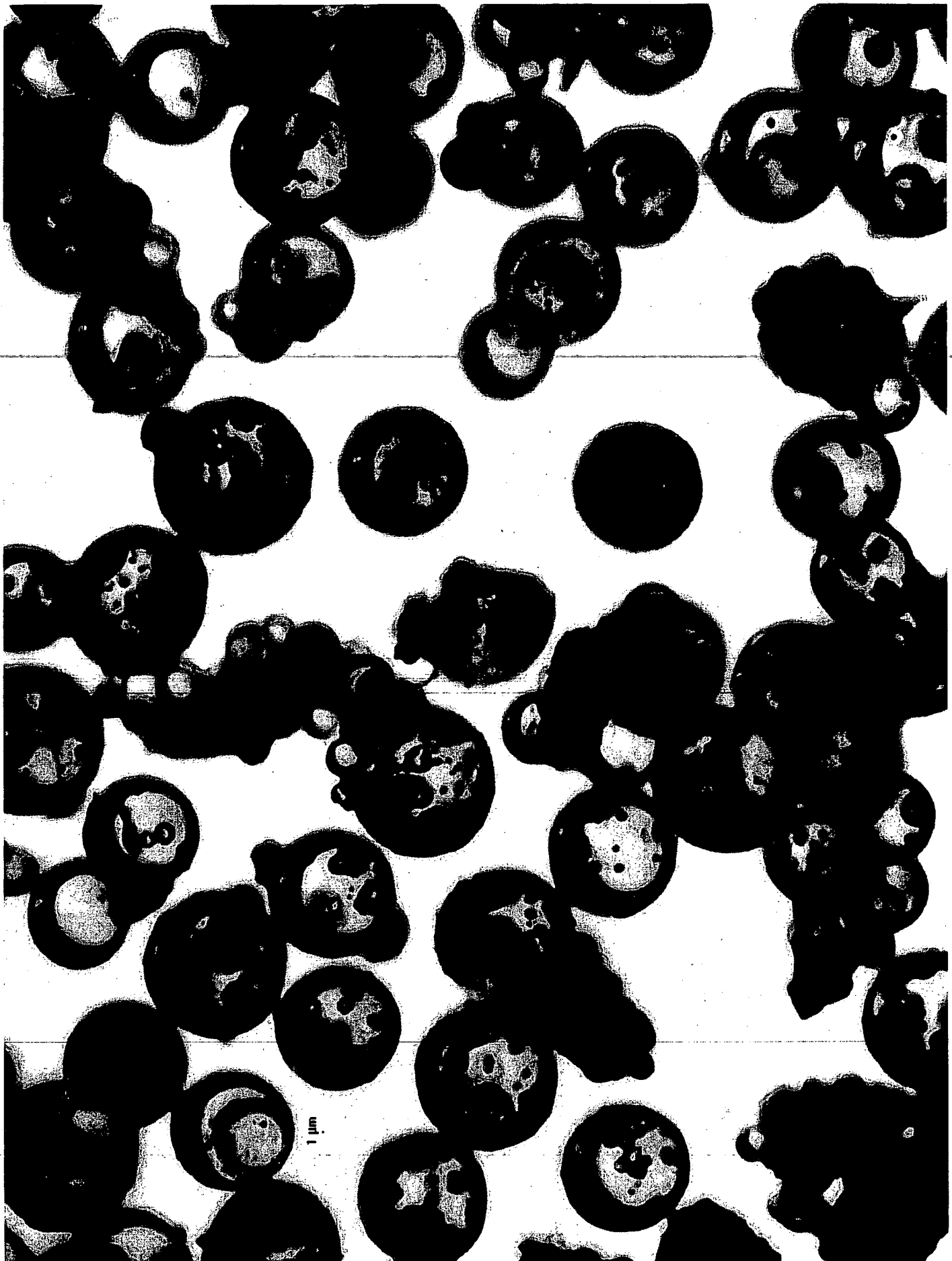
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Figure 4



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Figure 5



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